REMARKS

Claims 1-32 are pending in this application. Claims 1-32 have been canceled herewith without prejudice or disclaimer of the subject matter contained therein. Applicants note that claims 1-32 have not been cancelled for any reason related to patentability. Applicants reserve the right to pursue the subject matter of these claims in this or a future related application.

Claims 33-70 have been newly added. Support for the newly added claims can be found throughout the application as filed.

No new matter is added by way of these amendments to the claims.

CONCLUSIONS

Upon entry of this amendment, claims 33-70 will be pending in this application.

Please charge any requisite fees that are due, or credit any overpayments, to our Deposit Account No. 08-0219.

If a telephonic interview would advance prosecution of this application, the Examiner is invited to telephone the undersigned at the telephone number given below.

Respectfully submitted,

Dated: October 18, 2005

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MARKED-UP VERSION OF AMENDMENTS TO PENDING CLAIMS

1. (Currently Amended): A method for inducing tolerance in a patient to a graft from a mismatched donor, comprising:

depleting immune cells of the patient;

disrupting sex steroid-mediated signaling in the patient; ~~and~~

administering cells from the donor to the patient, wherein the cells are selected from the group consisting of stem cells, progenitor cells, and combinations thereof; and

analyzing the reactivity of T cells of the patient to cells from the donor or MHC matched to the donor, wherein the T cells have decreased responsiveness to donor or MHC matched cells compared to the responsiveness of the patient's T cells prior to treatment,

wherein the patient has increased tolerance to ~~a~~ the donor graft ~~is induced in the patient~~ compared to an untreated patient.

2. (Currently Amended): A method for inducing tolerance in a patient to a graft from a mismatched donor, comprising:

depleting immune cells of the patient;

disrupting sex steroid-mediated signaling in the patient, wherein the functionality of the bone marrow of the patient is increased without, prior to, or concurrently with, reactivation of the patient's ~~thymus, and~~ thymus;

administering cells from the donor to the patient, wherein the cells are selected from the group consisting of stem cells, progenitor cells, and combinations thereof; and

analyzing the reactivity of T cells of the patient to cells from the donor or MHC matched to the donor, wherein the T cells have decreased responsiveness to donor or MHC matched cells compared to the responsiveness of the patient's T cells prior to treatment

wherein the patient has increased ~~tolerance is induced in the~~ tolerance to the donor graft compared to an untreated patient.

3. (Currently Amended): A method for inducing tolerance in a patient to a graft from a mismatched donor, comprising:

depleting immune cells of the patient;

disrupting sex steroid-mediated signaling in the patient;

administering cells from the donor to the patient, wherein the cells are selected from the group consisting of stem cells, progenitor cells, and combinations ~~thereof; and~~ thereof;

allowing donor cell engraftment in the patient's bone marrow, wherein the donor cell engraftment is enhanced without, prior to, or concurrently with thymus reactivation; and

analyzing the reactivity of T cells of the patient to cells from the donor or MHC matched to the donor, wherein the T cells have decreased responsiveness to donor or MHC matched cells compared to the responsiveness of the patient's T cells prior to treatment,

wherein the patient has increased ~~tolerance is induced in the~~ tolerance to the donor graft compared to an untreated patient.

4. The method of any one of claims 1-3, wherein the thymus of the patient has been at least in part atrophied.

5. The method of claim 4, wherein the patient has a disease that at least in part atrophied the thymus of the patient.

6. The method of claim 4, wherein the patient has had a treatment of a disease that at least in part atrophied the thymus of the patient.

7. (Currently Amended): The method of claim ~~5~~ 6, wherein the treatment of the disease is immunosuppression, chemotherapy, or radiation treatment.

8. The method of any one of claims 1-3, wherein the stem cells are selected from the group consisting of hematopoietic stem cells, epithelial stem cells, and combinations thereof.

9. The method of any one of claims 1-3, wherein the progenitor cells are selected from the group consisting of lymphoid progenitor cells, myeloid progenitor cells, and combinations thereof.

10. The method of claim 8, wherein the cells are hematopoietic stem cells.

11. The method of claim 10, wherein the hematopoietic stem cells are $CD34^+$.

12. The method of claim 1 or 2, wherein the cells are administered at the time disruption of sex steroid-mediated signaling is begun.

13. (Currently Amended): The method of any one of claims 1-3, further comprising administering to the patient a substance selected from the group consisting of at least one cytokine, at least one hematopoietin, at least one lymphokine, at least one interleukin, at least one CSF, at least one growth factor, ~~or a combination of at least one cytokine and at least one growth factor to the patient~~ and a combination thereof.

14. (Currently Amended): The method of claim 13, wherein the cytokine is selected from the group consisting of Interleukin 1 (IL-1), Interleukin 2 (IL-2), Interleukin 3 (IL-3), Interleukin 4 (IL-4), Interleukin 5 (IL-5), Interleukin 6 (IL-6), Interleukin 7 (IL-7), Interleukin 8 (IL-8), Interleukin 9 (IL-9), Interleukin 10 (IL-10), Interleukin 11 (IL-11), Interleukin 12 (IL-12), Interleukin 13 (IL-13), Interleukin 15 (IL-15), ~~stem cell factor (SCF),~~ Interferon gamma (IFN-γ), and combinations thereof.

15. (Currently Amended): The method of claim 13, wherein the growth factor is selected from the group consisting of members of the epithelial growth factor family, members of the fibroblast growth factor family, stem cell factor, granulocyte colony stimulating factor (G-CSF), keratinocyte growth factor (KGF), granulocyte-macrophage colony stimulating factor (GM-

CSF), insulin-like growth factor-1 (IGF-1), a growth hormone, a thyroid hormone, M-CSF, Meg-CSF, MIF, LIF, TNF, PDGF, human growth hormone, B cell growth factor, B cell differentiation factor, eosinophil differentiation factor, and combinations thereof.

16. The method of any one of claims 1-3, wherein the sex steroid-mediated signaling is disrupted by castration.

17. The method of claim 16, wherein the sex steroid-mediated signaling is disrupted by surgical castration.

18. The method of claim 16, wherein the sex steroid-mediated signaling is disrupted by chemical castration.

19. The method of claim 18, wherein the sex steroid-mediated signaling is disrupted by administration of one or more pharmaceuticals.

20. (Currently Amended): The method of claim 19, wherein the one or more pharmaceuticals is selected from the group consisting of LHRH agonists, LHRH antagonists, anti-LHRH vaccines, anti-androgens, anti-estrogens, SERMs, SARMs, SPRMs, ERDs, aromatase inhibitors, adrenal gland blockers, aldosterone antagonists, antiprogestogens, progestins, antiprogestins, dioxalan derivatives, and combinations thereof.

21. (Currently Amended): The method of claim 20, wherein the LHRH agonists are selected from the group consisting of ~~eulexin,~~ goserelin, leuprolide, lupron, ~~dioxalan derivatives~~, triptorelin, meterelin, buserelin, histrelin, nafarelin, lutrelin, leuprorelin, deslorelin, cystorelin, decapeptyl, gonadorelin, and acetates, citrates and other salts thereof, and combinations thereof.

22. (Currently Amended): The method of claim ~~120~~ 20, wherein the LHRH antagonists are selected from the group consisting of abarelix, cetrorelix, acetates, citrates, and other salts thereof, and combinations thereof.

23. (Currently Amended): The method of claim 20, wherein the anti-androgen is selected from the group consisting of Cosudex®, bicalutamide, cyproterone acetate, liarozole, ketoconazole, flutamide, megestrol acetate, dutasteride, finasteride, eulexin, and combinations thereof.

24. The method of claim 20, wherein the anti-estrogen is selected from the group consisting of anastrozole, fulvestrant, tamoxifen, clomiphene, diethylstilbestrol, diethylstilbestrol diphosphate, danazol, droloxifene, iodoxyfene, toremifene, raloxofene, and combinations thereof.

25. (Currently Amended): The method of claim 20, wherein the adrenal gland blocker is selected from the group consisting of aminoglutethimide, formestane, vorazole, exemestane, anastrozole, letrozole, ~~and~~ exemestane, and combinations thereof.

26. (Cancelled): ~~The method of any one of claims 1-3, wherein the tolerance is induced to a donor graft.~~

27. (Currently Amended): The method of ~~claim 26~~ any one of claims 1-3, wherein the donor graft is selected from the group consisting of cells of the donor, tissues of the donor, organs of the donor, ~~or~~ and combinations thereof.

28. (New): The method of any one of claims 1-3, wherein the sex steroid-mediated signaling to the thymus is disrupted by lowering the level of a sex steroid hormone.

29. (New): The method of any one of claims 1-3, where the cells from the mismatched donor are genetically modified.

30. (New): The method of any one of claims 1-3, wherein the method results in the generation of a chimera selected from the group consisting of a chimeric thymus, chimeric hemopoietic cells, chimeric lymphoid cells, chimeric T cells, chimeric B cells, chimeric dendritic cells, a chimeric lymphoid organ, and any combination thereof.

31. (New): The method of any one of claims 1-3, further comprising an allograft transplantation of a graft having the same histocompatibility as that of the mismatched donor to the patient.

32. (New): The method of any one of claims 1-3, wherein the method comprises collecting blood samples from the patient from about 2 days to about 21 days after administering cells from the donor to the patient.